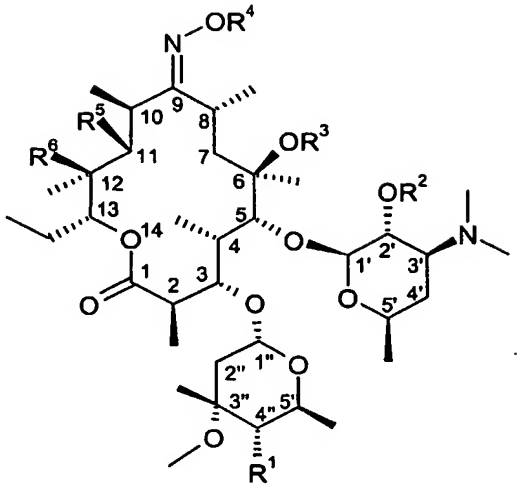
Claims

1. A compound of general formula (I)



(I)

wherein

R^1 is $OC(O)(CH_2)_mXR^7$;

R^2 is hydrogen or a hydroxyl protecting group;

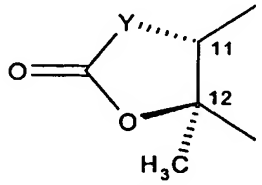
R^3 is hydrogen, C_{1-4}alkyl or C_{3-6}alkenyl optionally substituted by 9 to 10 membered fused bicyclic heteroaryl;

R^4 is hydrogen, C_{1-4}alkyl, C_{3-7}cycloalkyl, C_{3-6}alkenyl or a 5 or 6 membered heterocyclic group, wherein the alkyl, cycloalkyl, alkenyl and heterocyclic groups are optionally substituted by up to three substituents independently selected from optionally substituted 5 or 6 membered heterocyclic group, optionally substituted 5 or 6 membered heteroaryl, OR^8, $S(O)_nR^8$, NR^8R^9, $CONR^8R^9$, halogen and cyano;

R^5 is hydroxy, C_{3-6}alkenyloxy optionally substituted by 9 to 10 membered fused bicyclic heteroaryl, or $O(CH_2)_pO(CH_2)_qR^{10}$,

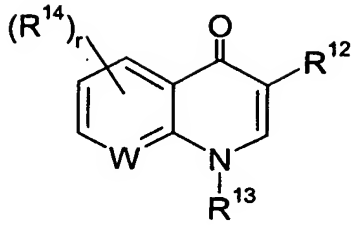
R^6 is hydroxy, or

R^5 and R^6 taken together with the intervening atoms form a cyclic group having the following structure:

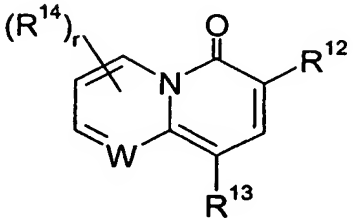


wherein Y is a bivalent radical selected from $-CH_2-$, -CH(CN)-, -O-, $-N(R^{11})-$ and $-CH(SR^{11})-$;

R^7 is a heterocyclic group having the following structure:



or



R^8 and R^9 are each independently selected from hydrogen and C_{1-4}alkyl;

R^{10} is hydrogen or NR^8R^9;

R^{11} is hydrogen or C_{1-4}alkyl substituted by a group selected from optionally substituted phenyl, optionally substituted 5 or 6 membered heteroaryl and optionally substituted 9 to 10 membered fused bicyclic heteroaryl;

R^{12} is hydrogen, $C(O)OR^{15}$, $C(O)NHR^{15}$ or $C(O)CH_2NO_2$;

R^{13} is hydrogen, C_{1-4}alkyl optionally substituted by hydroxy or C_{1-4}alkoxy, C_{3-7}cycloalkyl, or optionally substituted phenyl or benzyl;

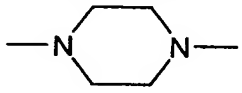
R^{14} is halogen, C_{1-4}alkyl, C_{1-4}thioalkyl, C_{1-4}alkoxy, NH_2, $NH(C_{1-4}alkyl)$ or $N(C_{1-4}alkyl)_2$;

R^{15} is hydrogen or C_{1-4}alkyl optionally substituted by up to three groups independently selected from halogen, C_{1-4}alkoxy, $OC(O)C_{1-4}$alkyl and $OC(O)OC_{1-4}$alkyl;

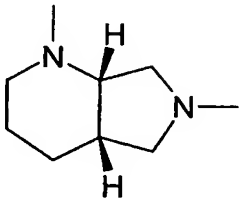
R^{16} is hydrogen, C_{1-4}alkyl, C_{3-7}cycloalkyl, optionally substituted phenyl or benzyl, acetyl or benzoyl;

R^{17} is hydrogen or R^{14}, or R^{17} and R^{13} are linked to form the bivalent radical $-O(CH_2)_2-$ or $-(CH_2)_v-$;

X is $-U(CH_2)_sZ-$ or X is a group selected from:



and



U and Z independently are a divalent radical selected from $-N(R^{16})-$, $-O-$, $-S(O)_t-$, $-N(R^{16})C(O)-$, $-C(O)N(R^{16})-$ and $-N[C(O)R^{16}]-$;

W is CR^{17} or a nitrogen atom;

m is 0 or an integer from 1 to 5;

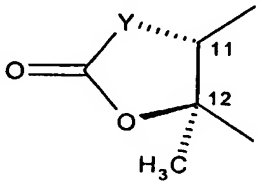
n, r and t are each independently selected from 0, 1 and 2;
p and q are each independently selected from 1 to 6 ;
s is an integer from 2 to 8; and
v is 2 or 3;
and pharmaceutically acceptable derivatives thereof.

2. A compound according to claim 1 wherein R^2 is hydrogen.

3. A compound according to claim 1 or 2 wherein R^3 is hydrogen.

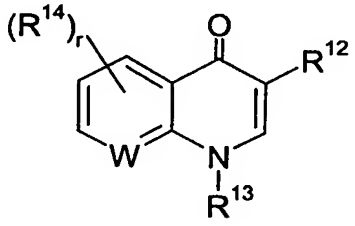
4. A compound according to any one of the preceding claims wherein R^4 is hydrogen or C_{1-4}alkyl optionally substituted by up to three substituents independently selected from optionally substituted 5 or 6 membered heteroaryl, OR^8, $S(O)_nR^8$, NR^8R^9, halogen and cyano.

5. A compound according to any one of the preceding claims wherein R^5 is hydroxy or $O(CH_2)_pO(CH_2)_qR^{10}$ and R^6 is hydroxy, or R^5 and R^6 taken together with the intervening atoms form a cyclic group having the following structure:



wherein Y is the bivalent radical -O-.

6. A compound according to any one of the preceding claims wherein R^7 is a heterocyclic group having the following structure:



wherein W is CR^{17} where R^{17} is hydrogen.

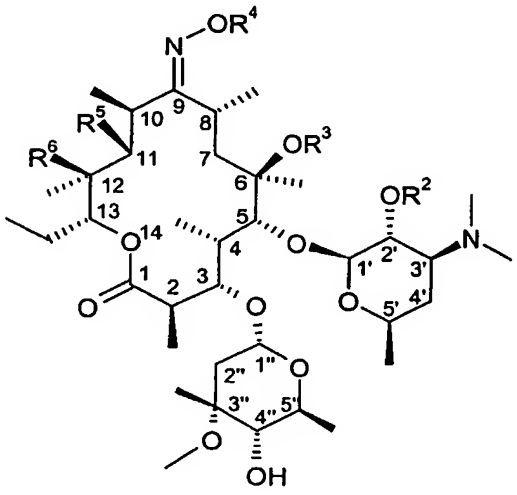
7. A compound according to any one of the preceding claims wherein X is $-U(CH_2)_sZ-$ wherein U and Z are independently -NH- or -O-.

8. A compound according to claim 1 as defined in any one of Examples 1 to 15, or a pharmaceutically derivative thereof.

9. A compound selected from:

4"-*O*-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinolinyl) amino]ethyl]amino]propionyl]-11-*O*-(2-dimethylaminoethoxymethyl)-(9E)-methoximino erythromycin A,
4"-*O*-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinolinyl) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-*O*-(2-propyl)oximino erythromycin A,
4"-*O*-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinolinyl) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-methoximino erythromycin A, and
4"-*O*-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinolinyl) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-*O*-(ethoxymethyl)oximino erythromycin A,
or a pharmaceutically acceptable derivative thereof.

10. A process for the preparation of a compound as claimed in claim 1 which comprises:
a) reacting a compound of formula (II)



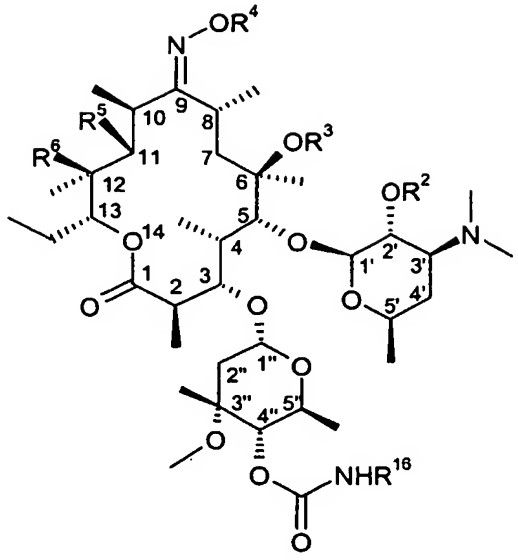
(II)

$HOC(O)(CH_2)_mX^aR^{7a}$
(III)

with a suitable activated derivative of the acid (III), wherein m is an integer 1 to 5, X^a and R^{7a} are X and R^7 as defined in claim 1 or groups convertible to X and R^7, to produce a compound of formula (I) wherein m is an integer 1 to 5;

b) reacting a compound of formula (II), in which the 4" hydroxy is suitably activated, with a compound of formula X^aR^{7a} (IV), wherein R^{7a} is R^{7a} as defined in claim 1 or a group convertible to R^7, s and Z have the meanings defined in claim 1 and X^a is $-U(CH_2)_sZ-$ or a group convertible to $-U(CH_2)_sZ-$, in which U is a group selected from selected from -$N(R^{16})-$, -O-, and -S-, to produce a compound of formula (I) wherein m is 0 and U is a group selected from -$N(R^{16})-$, -O- and -S-;

c) reacting a compound of formula (V)

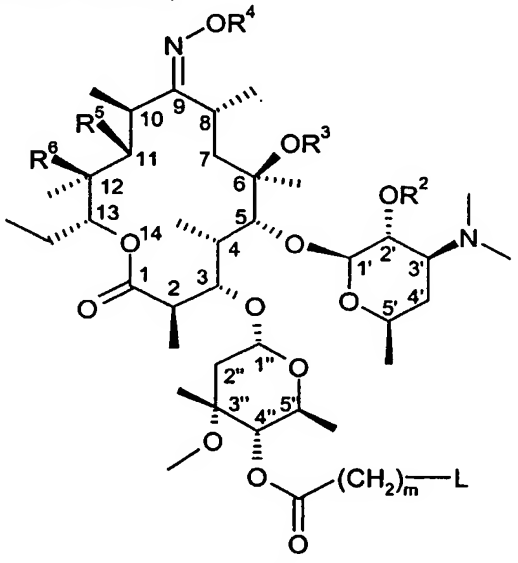


(V)

wherein R^{16} has the meaning defined in claim 1 with a suitable activated derivative of the carboxylic acid $HOC(O)(CH_2)_sZ^aR^{7a}$ (VI), wherein R^{7a} and Z^a are R^7 and Z as defined in claim 1 or groups convertible to R^7 and Z, to produce a compound of formula (I) wherein m is 0 and U is $-N(R^{16})C(O)-$;

d) reacting a compound of formula (II) with a suitably activated derivative of the carboxylic acid $HOC(O)C(O)N(R^{16})(CH_2)_sZ^aR^{7a}$ (VIIb) to produce a compound of formula (I) wherein m is 0 and U is $-C(O)N(R^{16})-$;

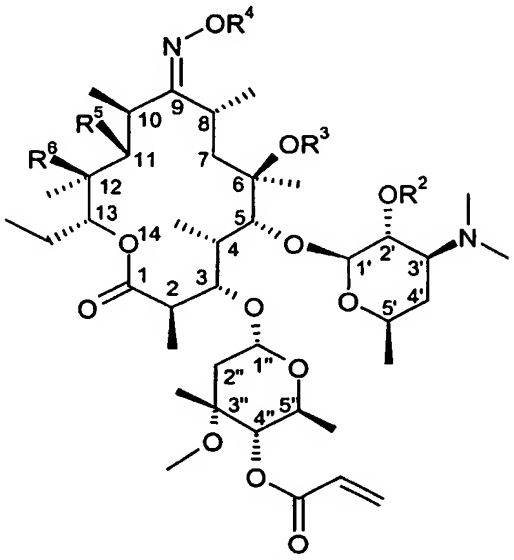
e) reacting a compound of formula (VII)



(VII)

with a compound of formula X^aR^{7a} (IV), wherein R^{7a} and X^a are R^7 and X as defined in claim 1 or groups convertible to R^7 and X, U is a group selected from $-N(R^{16})-$, -O- and -S-, and L is suitable leaving group, to produce a compound of formula (I) wherein m is 1 to 5 and U is a group selected from $-N(R^{16})-$, -O- and -S-; or

f) reacting a compound of formula (IX), with a compound of formula X^aR^{7a} (IV),



(IX)

wherein R^{7a} and X^a are R^7 and X as defined in claim 1 or groups convertible to R^7 and X, U is a group selected from -N(R^{16})-, -O- and -S-, to produce a compound of formula (I) wherein m is 2 and U is a group selected from -N(R^{16})-, -O- and -S-;

and thereafter, if required, subjecting the resulting compound to one or more of the following operations:

i) removal of the protecting group R^2,

ii) conversion of X^aR^{7a} or Z^aR^{7a} to XR^7 or ZR^7 respectively, and

iii) conversion of the resultant compound of formula (I) into a pharmaceutically acceptable derivative thereof.

11. A compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof for use in therapy.

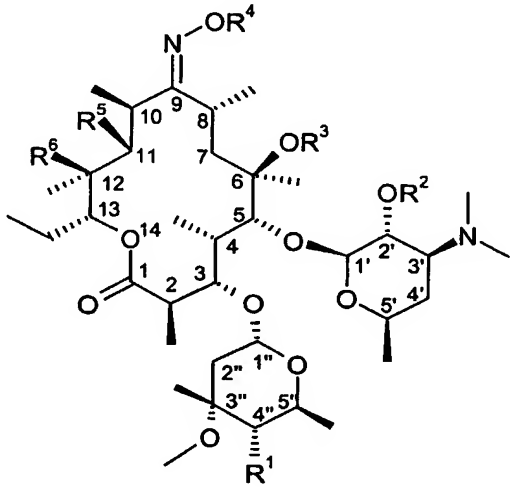
12. The use of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof in the preparation of a medicament for use in the therapy of systemic or topical microbial infections in a human or animal body.

13. The use of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof for use in the treatment or prophylaxis of systemic or topical microbial infections in a human or animal body.

14. A pharmaceutical composition comprising a compound as claimed any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof in admixture with one or more pharmaceutically acceptable carriers or excipients.

15. A method for the treatment of the human or non-human animal body to combat microbial infection comprising administration of an effective amount of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof.

16. A compound of general formula (IA)



(IA)

wherein

R^1 is $OC(O)(CH_2)_mXR^7$;

R^2 is hydrogen or a hydroxyl protecting group;

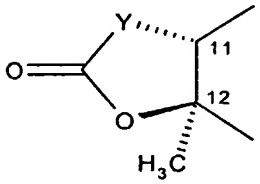
R^3 is hydrogen, C_{1-4}alkyl or C_{3-6}alkenyl optionally substituted by 9 to 10 membered fused bicyclic heteroaryl;

R^4 is hydrogen, C_{1-4}alkyl, C_{3-7}cycloalkyl, C_{3-6}alkenyl or a 5 or 6 membered heterocyclic group, wherein the alkyl, cycloalkyl, alkenyl and heterocyclic groups are optionally substituted by up to three substituents independently selected from optionally substituted 5 or 6 membered heterocyclic group, optionally substituted 5 or 6 membered heteroaryl, OR^8, $S(O)_nR^8$, NR^8R^9, $CONR^8R^9$, halogen and cyano;

R^5 is hydroxy, C_{3-6}alkenyloxy optionally substituted by 9 to 10 membered fused bicyclic heteroaryl or $O(CH_2)_pO(CH_2)_qR^{10}$,

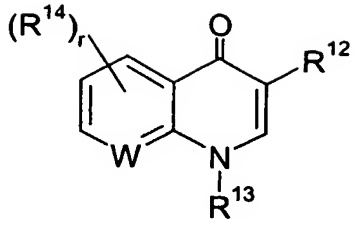
R^6 is hydroxy, or

R^5 and R^6 taken together with the intervening atoms form a cyclic group having the following structure:

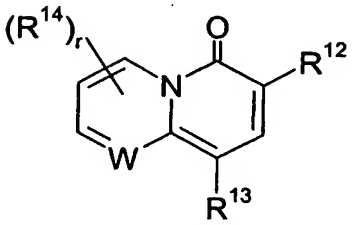


wherein Y is a bivalent radical selected from $-CH_2-$, -CH(CN)-, -O-, $-N(R^{11})-$ and $-CH(SR_8)-$;

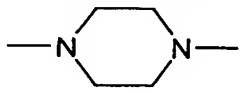
R^7 is a heterocyclic group having the following structure:



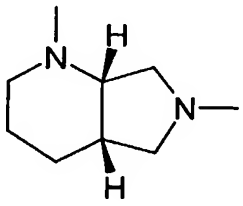
or



R^8 and R^9 are each independently selected from hydrogen and C_{1-4}alkyl;
R^{10} is hydrogen or NR^8R^9;
R^{11} is hydrogen or C_{1-4}alkyl substituted by a group selected from optionally substituted phenyl, optionally substituted 5 or 6 membered heteroaryl and optionally substituted 9 to 10 membered fused bicyclic heteroaryl;
R^{12} is hydrogen, $C(O)OR^{15}$, $C(O)NHR^{15}$ or $C(O)CH_2NO_2$;
R^{13} is hydrogen, C_{1-4}alkyl, C_{3-7}cycloalkyl, or optionally substituted phenyl or benzyl;
R^{14} is halogen, C_{1-4}alkyl, C_{1-4}thioalkyl, C_{1-4}alkoxy, NH_2, $NH(C_{1-4}alkyl)$ or $N(C_{1-4}alkyl)_2$;
R^{15} is hydrogen or C_{1-4}alkyl;
R^{16} is hydrogen, C_{1-4}alkyl, C_{3-7}cycloalkyl, optionally substituted phenyl or benzyl, acetyl or benzoyl;
X is $-U(CH_2)_sZ-$ or X is a group selected from:



and



U and Z independently are a divalent radical selected from $-N(R^{16})-$, -O-, $-S(O)_t-$, $N(R^{16})C(O)-$, $-C(O)N(R^{16})-$ and $-N[C(O)R^{16}]-$;
W is a carbon or a nitrogen atom;
m is 0 or an integer from 1 to 5;
n, r and t are each independently selected from 0, 1 and 2;
p and q are each independently selected from 1 and 2; and
s is an integer from 2 to 8;

and pharmaceutically acceptable salts and solvates thereof.